REMARKS

Applicants thank Examiner Wright for the courtesy of a telephonic interview on December 10, 2002. During the interview, the Examiner agreed to consider Applicants' arguments for why claim 24 should be examined on the merits in the present application and be allowable over the art of record.

Claims 1-39 are presently pending. Claims 1-23 where R_3 and R_4 taken together represent alkylidene or a heteroatom-containing alkylidene have been withdrawn from further consideration as being drawn to non-elected subject matter. Claims 1-3, 8, 9 and 17-19 have been amended to recite particular embodiments of the invention and to no longer recite non-elected subject matter. New claims 25-39 have been added to claim particular embodiments of the invention that read on the elected subject matter. Support for the amended and new claims is found in the specification at, for example, those portions set forth in Table 1, below. No new matter has been added. Claims 10-16 have been canceled without prejudice. Applicants reserve their right to prosecute the subject matter of any canceled claim in one or more continuation, continuation-in-part or divisional applications.

Table 1: Support for Amended or New Claims

Claim Number	Support
1	page 8, line 10 to page 9, line 9; page 9, lines 27-29
2	page 11, lines 15-20; page 9, lines 27-29
3	page 12, lines 1-5
8	page 8, lines 9-14; page 22, lines 19-20
9	page 23, lines 10-12; Example 8 (at page 52, line 5; page 53, line 4; and page 53, line 20)
17	page 8, lines 9-14
18	page 8, lines 9-14
19	page 8, lines 9-14
25	page 12, lines 1-5
26	page 8, lines 7-29
27	page 13, lines 17-20; page 15, lines 1-4
28	page 23, lines 10-12 and lines 24-25
29	page 23, lines 21-23
30	page 50, line 1, to page 52, line 3; Fig. 1
31	page 8, lines 7-9; page 50, lines 7-24
32	page 50, lines 8-12
33	page 11, lines 8-14
34	page 22, lines 20-22
35	page 23, lines 12-14
36	page 23, lines 12-23
37	page 23, lines 21-23
38	page 23, lines 4-5
39	page 50, lines 8-12

I. Claim 24 Must be Examined in the Present Application and is Patentable over the Art of Record

(a) Claim 24 Reads on Elected Group I and Must be Examined in the Present Application

Applicants respectfully traverse the withdrawal of claim 24 from consideration in the present application (Office Action, page 2, second line from the bottom, to page 3, line 2).

A Restriction Requirement (Paper No. 5) mailed September 25, 2001 in connection with the present application set forth three (3) groups:

Group I. Claims 1-24, drawn to compounds of claim 1, wherein R3 and R4 are the same or different and independently represent hydrogen, alkyl, cycloalkyl, aryl, arylalkyl, cycloalkylalkyl, aryloxyalkyl, alkoxyalkyl, alkoxyamino, or alkoxy(mono- or dialkylamino), and R1, R2, and R5 are as defined;

Group II. Claims 1-24, drawn to compounds of claim 1, wherein R3 and R4 are taken together and represent alkylidene or a heteroatom-containing alkylidene, wherein R3 and R4 comprise a six-membered ring, and R1, R2, and R5 are as defined; and

Group III. Claims 1-24, drawn to compounds of claim 1, wherein R3 and R4 are taken together and represent alkylidene or a heteroatom-containing alkylidene and wherein R3 and R4 comprise a ring which has seven or more members.

The Examiner has acknowledged (Office Action, page 2, lines 5-6) Applicants' election of Group I, claims 1-24, wherein R3 and R4 are the same or different and independently represent hydrogen, alkyl, cycloalkyl, aryl, arylalkyl, cycloalkylalkyl, aryloxyalkyl, alkoxyalkyl, alkoxyamino, or alkoxy(mono- or dialkylamino), and R1, R2, and R5 are as defined.

Group I reads not only on claims 1-23 where R3 and R4 are independently various substituents (R3 and R4 are relevant to -N(R3)(R4) and -NH-(alkyl)-N(R3)(R4), which are *optional* R1 or R2 substituents), *but also on claim 24* (Compound 1, the compound (or its pharmaceutically acceptable salt) recited in claim 24, does not have an R1 or R2 substituent). Accordingly, the Examiner must examine claim 24 in the present application

(*see* 37 C.F.R. § 1.143, last line ("If the [restriction] requirement is repeated and made final, the examiner will at the same time act on the claims to the invention elected.")). Therefore, Applicants believe that the withdrawal of claim 24 from consideration in the present application is improper, and that claim 24 should be examined on the merits in the present application.

(b) Claim 24 is Novel over the Cited Art

The Examiner has cited the following references against the claims:

STN International® CAPLUS Database, Accession No. 1997:491798, Ivanova et al. ("Ivanova");

STN International® CAPLUS Database, Accession No. 1994:30709, Sokolyuk et al. ("Sokolyuk");

STN International® CAPLUS Database, Accession No. 1973:406796, Arient et al. ("Arient");

U.S. Patent No. 4,198,518 to Tzikas ("Tzikas"); and

"Pyrazoloanthrone derivatives I. Reactivity of 3-aminopyraoloanthrone" Khimiya Geterotsiklicheskikh Soedinenii, Galushko et al. ("Galushko").

Neither Sokolyuk, Arient nor Tzikas discloses Compound 1 (or a pharmaceutically acceptable salt thereof), much less a composition comprising Compound 1 (or a pharmaceutically acceptable salt thereof) and a pharmaceutically acceptable carrier. Even if Ivanova and Galushko disclose Compound 1, neither Ivanova nor Galushko discloses a composition comprising Compound 1 (or a pharmaceutically acceptable salt thereof) and a pharmaceutically acceptable carrier. Accordingly, claim 24 is novel over Ivanova, Sokolyuk, Arient, Tzikas and Galushko.

(c) Claim 24 is Nonobvious over the Cited Art

In determining whether a case of prima facie obviousness exists, it is necessary to ascertain whether the prior art teachings would appear to be sufficient to one of ordinary skill in the art to suggest making the claimed substitution or other modification. *In re Lalu*, 747 F.2d 703, 705, 223 USPQ 1257, 1258 (Fed. Cir. 1984). It is insufficient to establish obviousness that the separate elements of the invention existed in the prior art, absent some teaching or suggestion, in the prior art, to combine the elements. *Ruiz v. A.B. Chance Co.*,

234 F.3d 654, 664, 57 USPQ2d 1167, 1167 (Fed. Cir. 2000) (quoting *Arkie Lures, Inc. v. Gene Larew Tackel, Inc.*, 119 F.3d 953, 957, 43 USPQ2d 1294, 1297 (Fed. Cir. 1997)).

Neither Ivanova, Sokolyuk, Arient, Tzikas nor Galushko, alone or in combination, disclose, much less suggest, a composition comprising Compound 1 (or a pharmaceutically acceptable salt thereof) *and a pharmaceutically acceptable carrier*. Neither Sokolyuk, Arient nor Tzikas even discloses Compound 1. Sokolyuk states merely "[t]he photochromism of 7-phenoxypyrazoleanthrones is complicated by their destruction to 7-hydroxypyrazoleanthrones" (Sokolyuk, Abstract). Arient merely provides a method for chemically synthesizing 5,8-dimethylpyrazolanthrone (Arient, Abstract). Tzikas relates to a process for making 3-substituted pyrazolanthrones that are allegedly useful as intermediates for the production of vat dyes, pigments and disperse dyes (Tzikas, Abstract and col. 2, lines 3-5). Ivanova discloses Compound 1, but states merely "XPS was used to investigate the electronic structures of pyrazolanthrone and its derivs. on the basis of quantum-chem. data" (Ivanova, Abstract). Galushko discloses Compound 1 and only some of its chemical properties (Galushko, page 777, Table 2, first entry). Accordingly, neither Sokolyuk, Arient, Tzikas, Ivanova nor Galushko, alone or in combination, suggests including Compound 1 (or a pharmaceutically acceptable salt thereof) in a composition comprising a pharmaceutically acceptable carrier. Therefore, neither Sokolyuk, Arient, Tzikas, Ivanova nor Galushko, alone or in combination, renders claim 24 obvious.

Thus, because claim 24 is novel and nonobvious over the art of record, claim 24 is allowable over the art of record.

(d) New Claim 39 is Novel and Nonobvious over the Cited Art

New claim 39 relates to a composition comprising the compound or a pharmaceutically acceptable salt of the compound of the composition of claim 24 and a JNK enzyme. Claim 39 is novel and nonobvious because there is no disclosure in any of the art of record of a composition comprising the compound of claim 24 and an enzyme, much less a JNK enzyme.

II. The Present Claims Do Not Recite Non-Elected Subject Matter

Claims 1-23 have been objected to for containing non-elected subject matter. The claims have been amended to no longer recite non-elected subject matter. In particular, claims 1 and 9 have been amended to delete the language "R_3 and R_4 taken together represent alkylidene or a heteroatom-containing alkylidene." Claims 2 and 3 have been

rewritten in independent form and do not recite that R_3 and R_4 can be taken together represent alkylidene or a heteroatom-containing alkylidene. Likewise, new compound claims 25-27 and new method claims 28-33 do not recite that R_3 and R_4 can be taken together represent alkylidene or a heteroatom-containing alkylidene. Claims 10-16 have been canceled without prejudice. Accordingly, Applicants believe that the objection to the for containing non-elected subject matter has been overcome and must be withdrawn.

III. The Present Claims are Novel over the Cited Art

Claims 1-4 and 8 have been rejected under 35 U.S.C. § 102(b) as being allegedly anticipated by Ivanova, Sokolyuk, Arient, Tzikas and Galushko. As explained below, the present claims are novel over these references.

Claim 1 has been amended to delete the recitation that R_1 and R_2 are independently alkyl, halogen, carboxyl, alkoxycarbonyl, alkoxy or aryloxy; replace "aryl" with "carbocyclic aromatic" and "heterocyclic aromatic" as R_5 variables; and added a proviso that carbocyclic aromatic is not phenyl. Claim 2 as amended now: (1) exists in independent form; (2) no longer recites that R_1 is alkyl, halogen or aryloxy; (3) no longer recites that R_2 is alkyl, halogen, carboxyl, alkoxy or aryloxy; (4) no longer recites that R_3 or R_4 is hydrogen; and (5) no longer recites that R_5 is phenyl. Claim 3 has been amended to delete the central structure depicted in the claim (*i.e.*, where optional substituents R_1 and R_2 are both on the phenyl ring that is not fused to the pyrazole ring).

New claim 25 relates to compounds wherein optional substituents R_1 and R_2 are both on the phenyl ring that is not fused to the pyrazole ring. Neither Galushko nor Tzikas discloses compounds with any substituents on this phenyl ring. Ivanova and Sokolyuk only disclose compounds with a chloro or phenyloxy substituent on this phenyl ring and Arient only discloses a compound with two methyl groups on this ring. New claim 25 does not recite that R_1 or R_2 can be alkyl, halogen or aryloxy. Accordingly, new claim 25 is novel over Sokolyuk, Arient, Tzikas, Ivanova and Galushko.

New claim 26 relates to compounds wherein optional substituents R_1 and R_2 are aminoalkylamino. None of Sokolyuk, Arient, Tzikas, Ivanova or Galushko discloses any compounds that have an aminoalkylamino group as set forth in new claim 26. Accordingly, new claim 26 is novel over Sokolyuk, Arient, Tzikas, Ivanova and Galushko.

New claim 27 relates to compounds with a single amino substituent on the phenyl ring that is fused to the pyrazole ring. The amino substituent must be on the carbon on the

"lower" portion of the phenyl ring (*i.e.*, on the non-fused carbon closest to the carbonyl group). None of Sokolyuk, Arient, Tzikas, Ivanova or Galushko discloses any compounds that have an amino substituent at this position. Accordingly, new claim 27 is novel over Sokolyuk, Arient, Tzikas, Ivanova and Galushko.

Ivanova discloses compounds wherein R_1 is chlorine, methyl or t-butyl and R_2 is absent. The amended claims do not read on these compounds.

Sokolyuk discloses compounds wherein R_1 is chlorine or phenyloxy and R_2 is absent. The amended claims do not read on these compounds.

Arient discloses compounds wherein R_1 is methyl and R_2 is methyl. The amended claims do not read on these compounds.

Tzikas discloses compounds wherein R_1 is C_1-C_6 alkyl, C_1-C_6 alkoxy, $-NH_2$, $-N(alkyl)_2$ or carboxy and R_2 is absent. The amended claims do not read on these compounds.

Galushko discloses compounds wherein R_1 is $-NH_2$, -NH(butyl) or -NH(C(O)phenyl) and R_2 is absent. The amended claims do not read on these compounds.

Accordingly, the rejection of claims 1-4 and 8 under 35 U.S.C. § 102(b) has been overcome, and should be withdrawn.

IV. The Present Claims are Nonobvious over the Cited Art

Claims 1-4 and 8 have been rejected under 35 U.S.C. § 103(a) as being allegedly obvious over Arient, Tzikas and Galushko. In particular, the Examiner has alleged that Arient and Tzikas teach examples and homologs of the presently claimed compounds and Galushko teaches an example and positional isomers of the presently claimed compounds.

As discussed above, the amended claims do not read on the compounds disclosed in Arient, Tzikas or Galushko. In addition, in view of the amendments discussed in connection with the § 102 rejection, neither Arient, Tzikas nor Galushko discloses a homolog of a presently claimed compound.

Even if Arient, Tzikas or Galushko does disclose a homolog or a positional isomer of a presently claimed compound, however, neither Arient, Tzikas nor Galushko, alone or in combination, renders the present claims obvious. An analysis of whether claimed compounds are obvious requires inquiry as to whether there is anything in a prior art reference suggesting the expected properties of the claimed compounds or whether the reference discloses any utility for its compounds that would support an expectation that the

claimed compounds would have similar properties. *Lalu*, 747 F.2d at 707, 223 USPQ at 1260; *In re Payne*, 606 F.2d 303, 313, 203 USPQ 245, 254 (CCPA 1979) (emphasis added) ("An obviousness rejection based on similarity in chemical structure and function entails the motivation of one skilled in the art to make a chemical compound, *in the expectation that compounds similar in structure will have similar properties.*"); *Yamanouchi Pharm. Co., Ltd. v. Danbury Pharmacal, Inc.*, 231 F.3d 1339, 1343, 56 USPQ2d 1641, 1644 (Fed. Cir. 2000) ("For a chemical compound, a prima facie case of obviousness requires 'structural similarity between claimed and prior art subject matter . . . where the prior art gives reason or motivation to make the claimed compositions'.") (quoting *In re Dillon*, 919 F.2d 688, 692, 16 USPQ2d 1897, 1901 (Fed. Cir. 1990)); *Ex parte Bonfils*, 64 USPQ2d 1456, 1463 (Bd. Pat. App. & Int'f 2002) (non-precedential) ("To the extent that Appellants intend to argue that the examiner has not established any basis for concluding that one of ordinary skill in the art would have had a reasonable expectation that the claimed compounds would have similar biological properties as the reference compounds, we agree that a *prima facie* case of obviousness has not been established . . . .").

Arient merely provides a method for chemically synthesizing 5,8-dimethylpyrazolanthrone (Arient, Abstract). Tzikas relates to a process for making 3-substituted pyrazolanthrones that are allegedly useful as intermediates for the production of vat dyes, pigments and disperse dyes (Tzikas, Abstract and col. 2, lines 3-5). Galushko discloses Compound 1 and only some of its chemical properties (Galushko, page 777, Table 2, first entry). Neither Arient, Tzikas nor Galushko, alone or in combination, teaches or suggests pharmaceutical uses, much less JNK inhibition. Accordingly, neither Arient, Tzikas nor Galushko, alone or in combination, renders the present claims obvious.

Therefore, it is believed that the rejection of claims 1-4 and 8 under 35 U.S.C. § 103(a) cannot stand and should be withdrawn.

V. Present Claim 9 is Enabled

Claim 9 has been rejected under 35 U.S.C. § 112, first paragraph, as allegedly not enabled.

Claim 9 has been amended to recite a method for inhibiting JNK *in vivo*. As discussed more fully below, the specification fully enables a method for inhibiting JNK *in vivo* for the following reasons: (1) the specification teaches that the compounds of the invention inhibit JNK; (2) the specification teaches pharmaceutical compositions

comprising a compound of the invention; (3) the specification teaches how to administer a compound of the invention or a pharmaceutical composition containing a compound of the invention to a patient in need thereof; and (4) the specification provides animal model data showing the beneficial effects resulting from the administration of a JNK inhibitor with respect to several unrelated disorders.

The specification teaches pharmaceutical compositions comprising a compound of the invention (see page 22, lines 19-28) and methods of administering a compound of the invention or pharmaceutical composition comprising a compound of the invention (see page 23, line 24 to page 24, line 4).

Furthermore, the specification provides *in vivo* data from several animal models demonstrating that the administration of a JNK inhibitor is beneficial for treating disorders such as lung inflammation (see page 52, line 24 to page 53, line 2), arthritis (see page 53, lines 4-18) and seizure (see page 53, line 20 to page 54, line 4).

Thus, in view of the above discussion, it is believed that the rejection of claim 9 under 35 U.S.C. § 112, first paragraph, has been overcome and must be withdrawn.

VI. Amended Claims 17-19

Claims 17-19 have been amended to refer to "the compound" of claim 9 "or a pharmaceutically acceptable salt thereof." Support for the amendments is set forth in Table 1, above. No new matter has been added.

VII. New Claims 25-39

New claims 25-39 have been added. New claims 25-27 relate to chemical compounds; new claims 28 and 29 relate to methods for treating a condition; new claims 29-32 relate to methods for inhibiting JNK; new claim 33 recites Compound 1 (or a pharmaceutically acceptable salt thereof); and new claims 34-39 relate to compositions. Support for new claims 25-37 is set forth in Table 1, above. New claims 25-39 read on the elected subject matter. No new matter has been added.

VIII. Claims 5-7 and 17-23 Should now be Allowable

Claims 5-7 and 10-23 were merely objected to. Independent claim 1, from which claims 5-7 depend, and independent claim 9, from which claims 17-23 depend (claims 10-16 have been canceled without prejudice), have been amended and are believed to be in

condition for allowance. Thus, Applicants believe claims 5-7 and 17-23 are now in condition for allowance.

IX. Conclusion

Applicants respectfully request that the present amendments be entered and the present remarks be made of record in the file history of the present application. An early allowance of the application is earnestly requested. The Examiner is invited to call the undersigned with any questions concerning the foregoing.

It is believed that no amendment fee is due, however, in the event any amendment fee is required, please charge the required fee to Pennie & Edmonds LLP Deposit Account No. 16-1150.

Respectfully submitted,

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By: Matthew E. Lamp, Ly. No. 36,343

Date December 18, 2002 35,203

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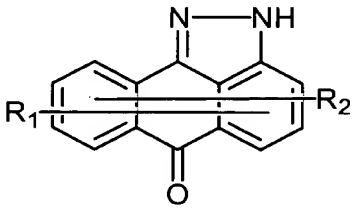
Enclosures

EXHIBIT A

U.S. PATENT APPLICATION SERIAL NO. 09/642,557
MARKED-UP VERSION OF ALL AMENDED CLAIMS

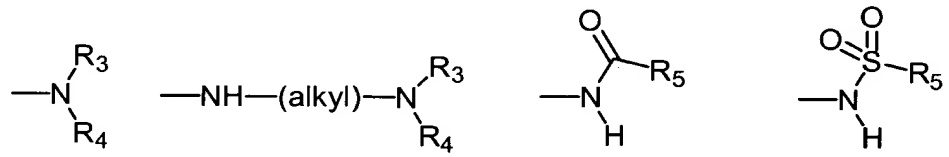
1. A compound having the structure:



or a pharmaceutically acceptable salt thereof,

wherein

R_1 and R_2 are optional substituents that are the same or different and independently represent [alkyl, halogen,] nitro, trifluoromethyl, sulfonyl, [carboxyl, alkoxycarbonyl, alkoxy,] aryl, [aryloxy,] arylalkyloxy, arylalkyl, cycloalkylalkyloxy, cycloalkyloxy, alkoxyalkyl, alkoxyalkoxy, aminoalkoxy, mono- or di-alkylaminoalkoxy, or a group represented by formula (a), (b), (c) or (d):



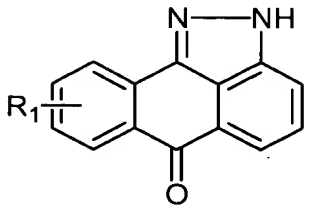
(a) (b) (c) (d)

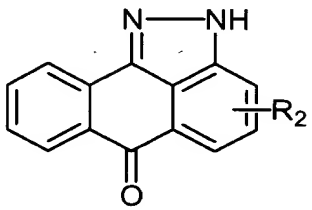
[R_3 and R_4 taken together represent alkylidene or a heteroatom-containing alkylidene, or] R_3 and R_4 are the same or different and independently represent [hydrogen, alkyl,] cycloalkyl, aryl, arylalkyl, cycloalkylalkyl, aryloxyalkyl, alkoxyalkyl, alkoxyamino, or alkoxy(mono- or di-alkylamino); and

R_5 represents hydrogen, alkyl, cycloalkyl, [aryl,] carbocyclic aromatic, heterocyclic aromatic, arylalkyl, cycloalkylalkyl, alkoxy, amino, mono- or di-alkylamino, arylamino, arylalkylamino, cycloalkylamino or cycloalkylalkylamino, with the proviso that carbocyclic aromatic is not phenyl;

and with the proviso that at least R_1 or R_2 is present.

2. [The] A compound [of claim 1 wherein R_1 or R_2 is present, and] having one of the following structures:

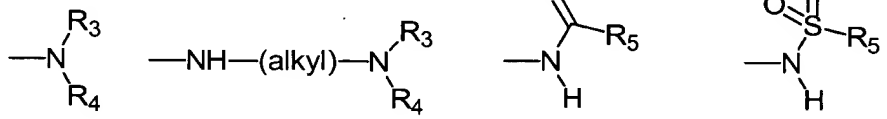




or a pharmaceutically acceptable salt thereof,

wherein

R_1 represents nitro, trifluoromethyl, sulfonyl, carboxyl, alkoxycarbonyl, alkoxy, aryl, arylalkyloxy, arylalkyl, cycloalkylalkyloxy, cycloalkyloxy, alkoxyalkyl, alkoxyalkoxy, aminoalkoxy, mono- or di-alkylaminoalkoxy, or a group represented by formula (a), (b), (c) or (d):



(a) (b) (c) (d)

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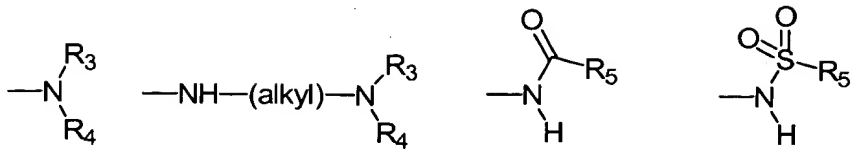
when R_1 is present, R_3 and R_4 are the same or different and independently represent hydrogen, alkyl, cycloalkyl, aryl, arylalkyl, cycloalkylalkyl, aryloxyalkyl, alkoxyalkyl, alkoxyamino, or alkoxy(mono- or di-alkylamino);

when R_1 is present, R_5 represents hydrogen, alkyl, cycloalkyl, aryl, arylalkyl, cycloalkylalkyl, alkoxy, amino, mono- or di-alkylamino, arylamino, arylalkylamino, cycloalkylamino or cycloalkylalkylamino;

R_2 represents nitro, trifluoromethyl, sulfonyl, alkoxycarbonyl, aryl, arylalkyloxy, arylalkyl, cycloalkylalkyloxy, cycloalkyloxy, alkoxyalkyl, alkoxyalkoxy, aminoalkoxy, mono- or di-alkylaminoalkoxy, or a group represented by formula (a), (b), (c) or (d):

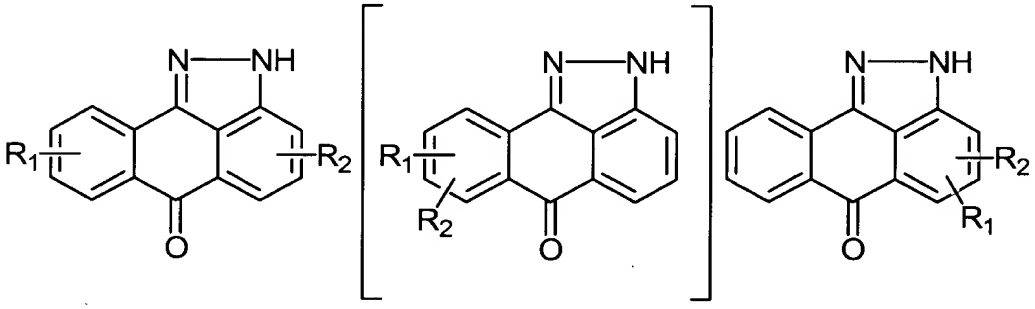


(a) (b) (c) (d)

when R_2 is present, R_3 and R_4 are the same or different and independently represent alkyl, cycloalkyl, aryl, arylalkyl, cycloalkylalkyl, aryloxyalkyl, alkoxyalkyl, alkoxyamino, or alkoxy(mono- or di-alkylamino); and

when R_2 is present, R_5 represents hydrogen, alkyl, cycloalkyl, carbocyclic aromatic, heterocyclic aromatic, arylalkyl, cycloalkylalkyl, alkoxy, amino, mono- or di-alkylamino, arylamino, arylalkylamino, cycloalkylamino or cycloalkylalkylamino with the proviso that carbocyclic aromatic is not phenyl.

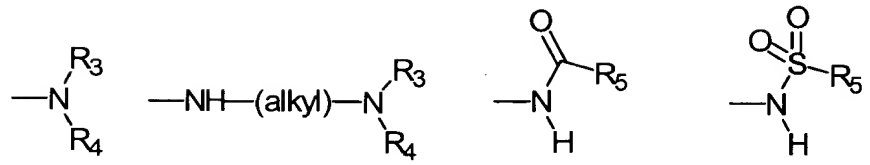
3. [The] A compound [of claim 1 wherein both R_1 and R_2 are present, and] having one of the following structures:



or a pharmaceutically acceptable salt thereof,

wherein

R_1 and R_2 represent alkyl, halogen, nitro, trifluoromethyl, sulfonyl, carboxyl, alkoxycarbonyl, alkoxy, aryl, aryloxy, arylalkyloxy, arylalkyl, cycloalkylalkyloxy, cycloalkyloxy, alkoxyalkyl, alkoxyalkoxy, aminoalkoxy, mono- or di-alkylaminoalkoxy, or a group represented by formula (a), (b), (c) or (d):



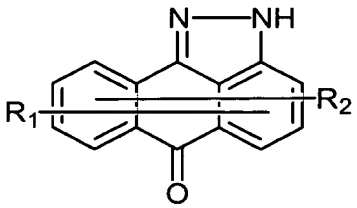
(a) (b) (c) (d)

R_3 and R_4 taken together represent alkylidene or a heteroatom-containing alkylidene, or R_3 and R_4 are the same or different and independently represent hydrogen, alkyl, cycloalkyl, aryl, arylalkyl, cycloalkylalkyl, aryloxyalkyl, alkoxyalkyl, alkoxyamino, or alkoxy(mono- or di-alkylamino); and

R_5 represents hydrogen, alkyl, cycloalkyl, aryl, arylalkyl, cycloalkylalkyl, alkoxy, amino, mono- or di-alkylamino, arylamino, arylalkylamino, cycloalkylamino or cycloalkylalkylamino.

8. (Amended) A composition comprising the compound or pharmaceutically acceptable salt of the compound of claim 1 and a pharmaceutically acceptable carrier.

9. (Amended) A method for [treating a condition responsive to] inhibiting JNK [inhibition] *in vivo*, comprising administering to a patient in need thereof an effective amount of a compound having the structure:

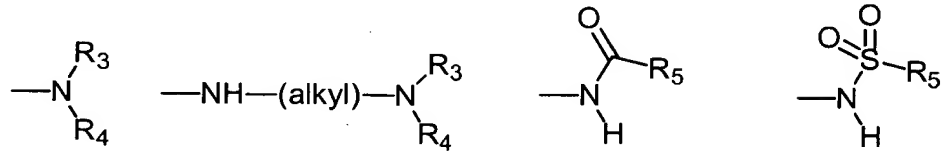


or a pharmaceutically acceptable salt thereof,

wherein

R_1 and R_2 are optional substituents that are the same or different and independently represent alkyl, halogen, nitro, trifluoromethyl, sulfonyl, carboxyl, alkoxycarbonyl, alkoxy, aryl, aryloxy, arylalkyloxy, arylalkyl, cycloalkylalkyloxy,

cycloalkyloxy, alkoxyalkyl, alkoxyalkoxy, aminoalkoxy, mono- or di-alkylaminoalkoxy, or a group represented by formula (a), (b), (c) or (d):

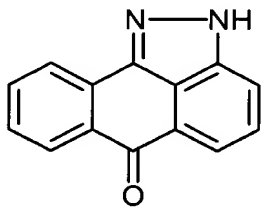


(a) (b) (c) (d)

[R_3 and R_4 taken together represent alkylidene or a heteroatom-containing alkylidene, or] R_3 and R_4 are the same or different and independently represent hydrogen, alkyl, cycloalkyl, aryl, arylalkyl, cycloalkylalkyl, aryloxyalkyl, alkoxyalkyl, alkoxyamino, or alkoxy(mono- or di-alkylamino); and

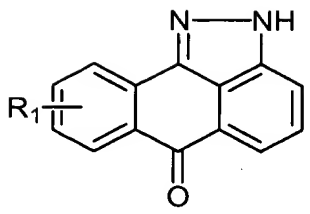
R_5 represents hydrogen, alkyl, cycloalkyl, aryl, arylalkyl, cycloalkylalkyl, alkoxy, amino, mono- or di-alkylamino, arylamino, arylalkylamino, cycloalkylamino, or cycloalkylalkylamino.

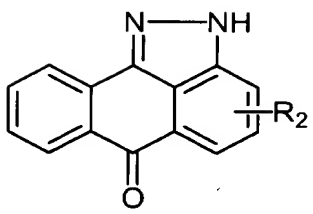
17. (Amended) The method of claim 9 wherein R_1 and R_2 are not present, and the compound having the following structure:



or a pharmaceutically acceptable salt thereof.

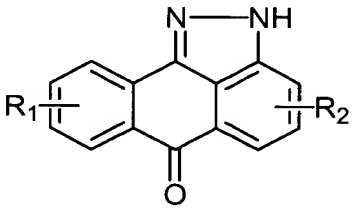
18. (Amended) The method of claim 9 wherein R_1 or R_2 is present, and the compound having one of the following structures:

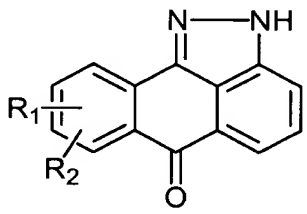


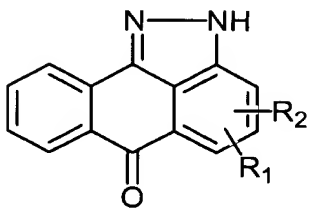


or a pharmaceutically acceptable salt thereof.

19. (Amended) The method of claim 9 wherein both R_1 and R_2 are present, and the compound having one of the following structures:



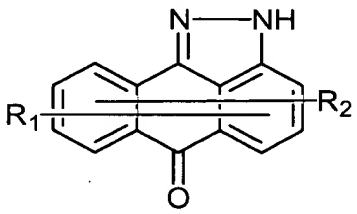




or a pharmaceutically acceptable salt thereof.

EXHIBIT B
U.S. PATENT APPLICATION SERIAL NO. 09/642,557
CLEAN VERSION OF CLAIMS UNDER CONSIDERATION
AFTER ENTRY OF PRESENT AMENDMENT

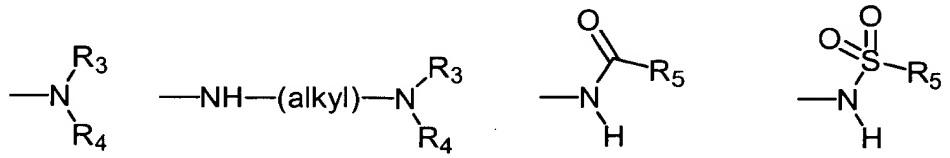
1. (Amended) A compound having the structure:



or a pharmaceutically acceptable salt thereof,

wherein

R_1 and R_2 are optional substituents that are the same or different and independently represent nitro, trifluoromethyl, sulfonyl, aryl, arylalkyloxy, arylalkyl, cycloalkylalkyloxy, cycloalkyloxy, alkoxyalkyl, alkoxyalkoxy, aminoalkoxy, mono- or di-alkylaminoalkoxy, or a group represented by formula (a), (b), (c) or (d):



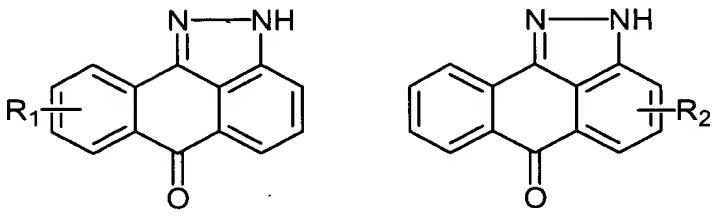
(a) (b) (c) (d)

R_3 and R_4 are the same or different and independently represent cycloalkyl, aryl, arylalkyl, cycloalkylalkyl, aryloxyalkyl, alkoxyalkyl, alkoxyamino, or alkoxy(mono- or di-alkylamino); and

R_5 represents hydrogen, alkyl, cycloalkyl, carbocyclic aromatic, heterocyclic aromatic, arylalkyl, cycloalkylalkyl, alkoxy, amino, mono- or di-alkylamino, arylamino, arylalkylamino, cycloalkylamino or cycloalkylalkylamino, with the proviso that carbocyclic aromatic is not phenyl;

and with the proviso that at least R_1 or R_2 is present.

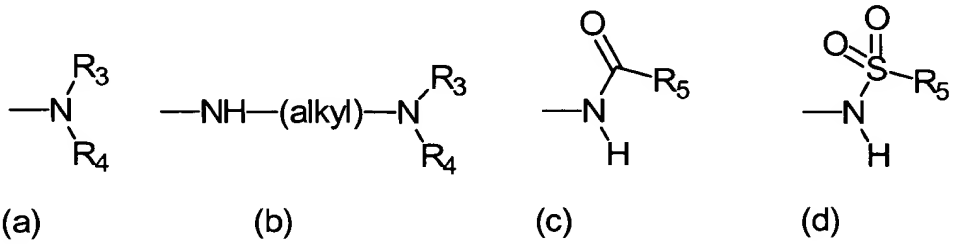
2. (Amended) A compound having one of the following structures:



or a pharmaceutically acceptable salt thereof,

wherein

R_1 represents nitro, trifluoromethyl, sulfonyl, carboxyl, alkoxycarbonyl, alkoxy, aryl, arylalkyloxy, arylalkyl, cycloalkylalkyloxy, cycloalkyloxy, alkoxyalkyl, alkoxyalkoxy, aminoalkoxy, mono- or di-alkylaminoalkoxy, or a group represented by formula (a), (b), (c) or (d):

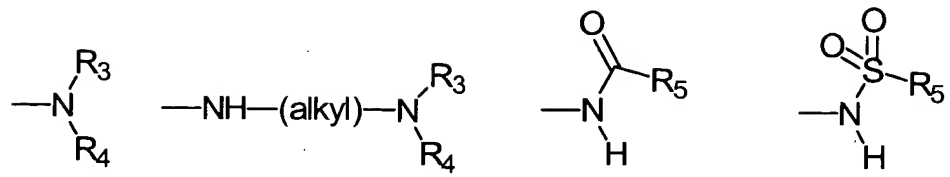


(a) (b) (c) (d)

when R_1 is present, R_3 and R_4 are the same or different and independently represent hydrogen, alkyl, cycloalkyl, aryl, arylalkyl, cycloalkylalkyl, aryloxyalkyl, alkoxyalkyl, alkoxyamino, or alkoxy(mono- or di-alkylamino);

when R_1 is present, R_5 represents hydrogen, alkyl, cycloalkyl, aryl, arylalkyl, cycloalkylalkyl, alkoxy, amino, mono- or di-alkylamino, arylamino, arylalkylamino, cycloalkylamino or cycloalkylalkylamino;

R_2 represents nitro, trifluoromethyl, sulfonyl, alkoxycarbonyl, aryl, arylalkyloxy, arylalkyl, cycloalkylalkyloxy, cycloalkyloxy, alkoxyalkyl, alkoxyalkoxy, aminoalkoxy, mono- or di-alkylaminoalkoxy, or a group represented by formula (a), (b), (c) or (d):

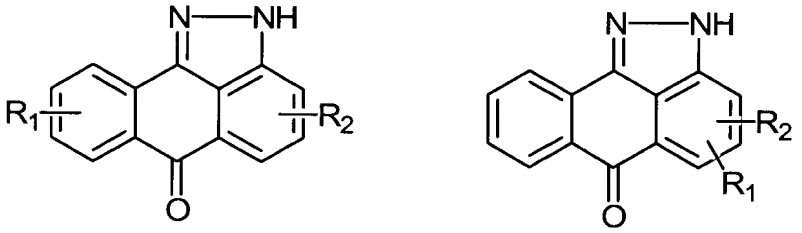


(a) (b) (c) (d)

when R_2 is present, R_3 and R_4 are the same or different and independently represent alkyl, cycloalkyl, aryl, arylalkyl, cycloalkylalkyl, aryloxyalkyl, alkoxyalkyl, alkoxyamino, or alkoxy(mono- or di-alkylamino); and

when R_2 is present, R_5 represents hydrogen, alkyl, cycloalkyl, carbocyclic aromatic, heterocyclic aromatic, arylalkyl, cycloalkylalkyl, alkoxy, amino, mono- or di-alkylamino, arylamino, arylalkylamino, cycloalkylamino or cycloalkylalkylamino with the proviso that carbocyclic aromatic is not phenyl.

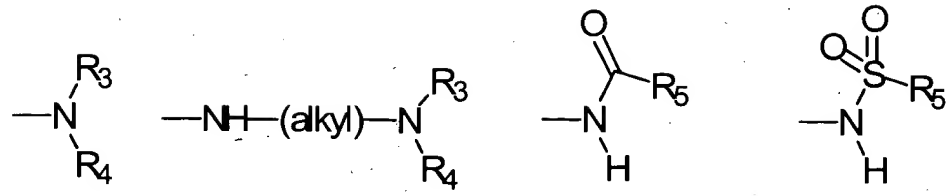
3. (Amended) A compound having one of the following structures:



or a pharmaceutically acceptable salt thereof,

wherein

R_1 and R_2 represent alkyl, halogen, nitro, trifluoromethyl, sulfonyl, carboxyl, alkoxycarbonyl, alkoxy, aryl, aryloxy, arylalkyloxy, arylalkyl, cycloalkylalkyloxy, cycloalkyloxy, alkoxyalkyl, alkoxyalkoxy, aminoalkoxy, mono- or di-alkylaminoalkoxy, or a group represented by formula (a), (b), (c) or (d):

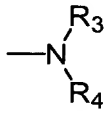


(a) (b) (c) (d)

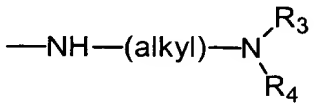
R_3 and R_4 taken together represent alkylidene or a heteroatom-containing alkylidene, or R_3 and R_4 are the same or different and independently represent hydrogen, alkyl, cycloalkyl, aryl, arylalkyl, cycloalkylalkyl, aryloxyalkyl, alkoxyalkyl, alkoxyamino, or alkoxy(mono- or di-alkylamino); and

R_5 represents hydrogen, alkyl, cycloalkyl, aryl, arylalkyl, cycloalkylalkyl, alkoxy, amino, mono- or di-alkylamino, arylamino, arylalkylamino, cycloalkylamino or cycloalkylalkylamino.

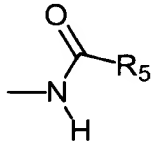
4. The compound of claim 2 wherein R_1 and R_2 are:



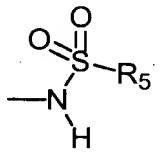
5. The compound of claim 2 wherein R_1 and R_2 are:



6. The compound of claim 2 wherein R_1 and R_2 are:

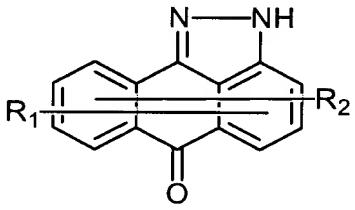


7. The compound of claim 2 wherein R_1 and R_2 are:



8. (Amended) A composition comprising the compound or pharmaceutically acceptable salt of the compound of claim 1 and a pharmaceutically acceptable carrier.

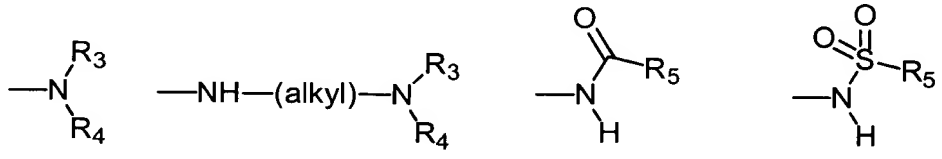
9. (Amended) A method for inhibiting JNK *in vivo*, comprising administering to a patient in need thereof an effective amount of a compound having the structure:



or a pharmaceutically acceptable salt thereof,

wherein

R_1 and R_2 are optional substituents that are the same or different and independently represent alkyl, halogen, nitro, trifluoromethyl, sulfonyl, carboxyl, alkoxycarbonyl, alkoxy, aryl, aryloxy, arylalkyloxy, arylalkyl, cycloalkylalkyloxy, cycloalkyloxy, alkoxyalkyl, alkoxyalkoxy, aminoalkoxy, mono- or di-alkylaminoalkoxy, or a group represented by formula (a), (b), (c) or (d):



(a) (b) (c) (d)

R_3 and R_4 are the same or different and independently represent hydrogen, alkyl, cycloalkyl, aryl, arylalkyl, cycloalkylalkyl, aryloxyalkyl, alkoxyalkyl, alkoxyamino, or alkoxy(mono- or di-alkylamino); and

R_5 represents hydrogen, alkyl, cycloalkyl, aryl, arylalkyl, cycloalkylalkyl, alkoxy, amino, mono- or di-alkylamino, arylamino, arylalkylamino, cycloalkylamino, or cycloalkylalkylamino.

10. The method of claim 9 wherein the condition is cancer.

11. The method of claim 9 wherein the condition is rheumatoid arthritis, rheumatoid spondylitis, osteoarthritis, gout, asthma, bronchitis, cystic fibrosis, inflammatory bowel disease, irritable bowel syndrome, mucous colitis, ulcerative colitis, Crohn's disease, gastritis, esophagitis, hepatitis, multiple sclerosis, endotoxin shock, psoriasis, eczema, or dermatitis.

12. The method of claim 9 wherein the condition is atherosclerosis, restenosis following angioplasty, left ventricular hypertrophy, or myocardial infarction.

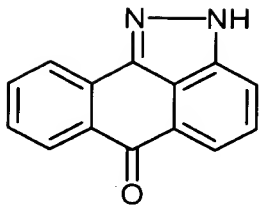
13. The method of claim 9 wherein the condition is stroke or ischemic damage to the heart, kidney, liver, or brain.

14. The method of claim 9 wherein the condition is transplant rejection.

15. The method of claim 9 wherein the condition is a central or peripheral neurological degenerative disorder.

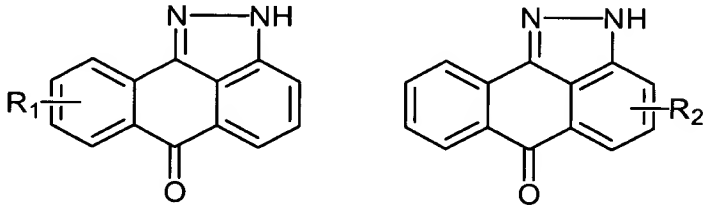
16. The method of claim 15 wherein the central or peripheral neurological degenerative disorder is epilepsy, Alzheimer's disease, Parkinson's disease, Huntington's disease, amyotrophic laterial sclerosis, a peripheral neuropathy, or spinal cord damage.

17. (Amended) The method of claim 9 wherein R_1 and R_2 are not present, and the compound having the following structure:



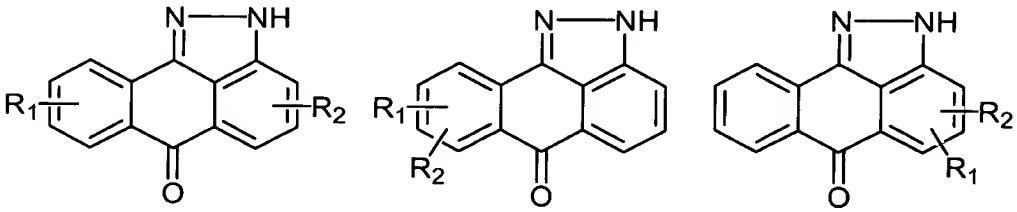
or a pharmaceutically acceptable salt thereof.

18. (Amended) The method of claim 9 wherein R_1 or R_2 is present, and the compound having one of the following structures:



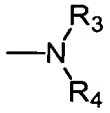
or a pharmaceutically acceptable salt thereof.

19. (Amended) The method of claim 9 wherein both R_1 and R_2 are present, and the compound having one of the following structures:

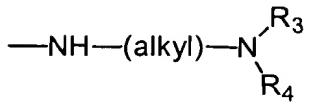


or a pharmaceutically acceptable salt thereof.

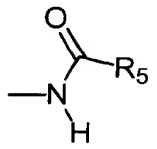
20. The method of claim 18 wherein R_1 and R_2 are:



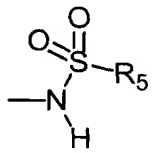
21. The method of claim 18 wherein R_1 and R_2 are:



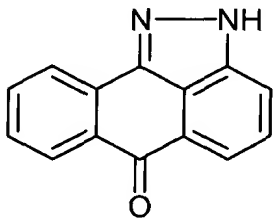
22. The method of claim 18 wherein R_1 and R_2 are:



23. The method of claim 18 wherein R_1 and R_2 are:

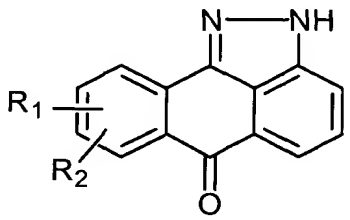


24. A composition comprising a compound having the structure:



or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

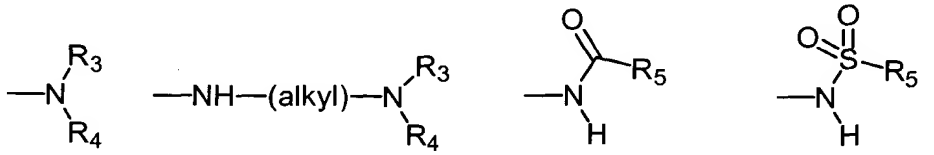
25. (New) A compound having the structure:



or a pharmaceutically acceptable salt thereof,

wherein

R_1 and R_2 are optional substituents that are the same or different and independently represent, nitro, trifluoromethyl, sulfonyl, carboxyl, alkoxycarbonyl, alkoxy, aryl, arylalkyloxy, arylalkyl, cycloalkylalkyloxy, cycloalkyloxy, alkoxyalkyl, alkoxyalkoxy, aminoalkoxy, mono- or di-alkylaminoalkoxy, or a group represented by formula (a), (b), (c) or (d):



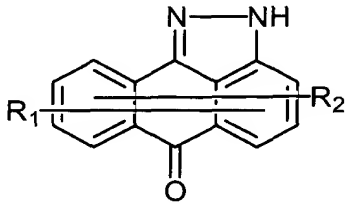
(a) (b) (c) (d)

R_3 and R_4 are the same or different and independently represent hydrogen, alkyl, cycloalkyl, aryl, arylalkyl, cycloalkylalkyl, aryloxyalkyl, alkoxyalkyl, alkoxyamino, or alkoxy(mono- or di-alkylamino); and

R_5 represents hydrogen, alkyl, cycloalkyl, aryl, arylalkyl, cycloalkylalkyl, alkoxy, amino, mono- or di-alkylamino, arylamino, arylalkylamino, cycloalkylamino or cycloalkylalkylamino;

and with the proviso that at least one of R_1 or R_2 is present.

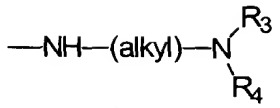
26. (New) A compound having the structure:



or a pharmaceutically acceptable salt thereof,

wherein

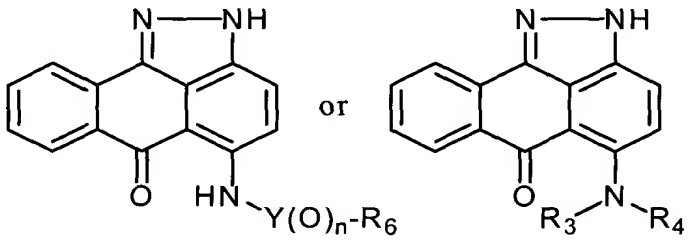
R_1 and R_2 are optional substituents that are the same or different and independently represent:



wherein R_3 and R_4 are the same or different and independently represent hydrogen, alkyl, cycloalkyl, aryl, arylalkyl, cycloalkylalkyl, aryloxyalkyl, alkoxyalkyl, alkoxyamino, or alkoxy(mono- or di-alkylamino);

and with the proviso that at least R_1 or R_2 is present.

27. (New) A compound having one of the following structures:



or a pharmaceutically acceptable salt thereof,

wherein

Y is C or S;

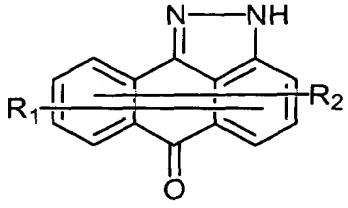
n is 1 when Y is C;

n is 2 when Y is S;

R_3 and R_4 are the same or different and independently represent hydrogen, alkyl, cycloalkyl, aryl, arylalkyl, cycloalkylalkyl, aryloxyalkyl, alkoxyalkyl, alkoxyamino, or alkoxy(mono- or di-alkylamino); and

R_6 represents phenyl, pyridinyl, thienyl or alkyl.

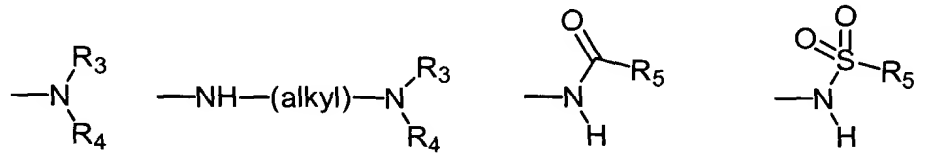
28. (New) A method for treating a condition, comprising administering to a patient in need thereof an effective amount of a compound having the structure:



or a pharmaceutically acceptable salt thereof,

wherein

R_1 and R_2 are optional substituents that are the same or different and independently represent alkyl, halogen, nitro, trifluoromethyl, sulfonyl, carboxyl, alkoxycarbonyl, alkoxy, aryl, aryloxy, arylalkyloxy, arylalkyl, cycloalkylalkyloxy, cycloalkyloxy, alkoxyalkyl, alkoxyalkoxy, aminoalkoxy, mono- or di-alkylaminoalkoxy, or a group represented by formula (a), (b), (c) or (d):



(a) (b) (c) (d)

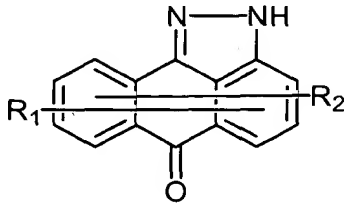
R_3 and R_4 are the same or different and independently represent hydrogen, alkyl, cycloalkyl, aryl, arylalkyl, cycloalkylalkyl, aryloxyalkyl, alkoxyalkyl, alkoxyamino, or alkoxy(mono- or di-alkylamino); and

R_5 represents hydrogen, alkyl, cycloalkyl, aryl, arylalkyl, cycloalkylalkyl, alkoxy, amino, mono- or di-alkylamino, arylamino, arylalkylamino, cycloalkylamino, or cycloalkylalkylamino,

the condition being cancer; rheumatoid arthritis; rheumatoid spondylitis; osteoarthritis; gout; asthma; bronchitis; cystic fibrosis; inflammatory bowel disease; irritable bowel syndrome; mucous colitis; ulcerative colitis; Crohn's disease; gastritis; esophagitis; hepatitis; multiple sclerosis; endotoxin shock; psoriasis; eczema; dermatitis; atherosclerosis; restenosis following angioplasty; left ventricular hypertrophy; myocardial infarction; stroke or ischemic damage to the heart, kidney, liver, or brain; transplant rejection; or a central or peripheral neurological degenerative disorder.

29. (New) The method of claim 28, wherein the central or peripheral neurological degenerative disorder is epilepsy, Alzheimer's disease, Parkinson's disease, Huntington's disease, amyotrophic laterial sclerosis, a peripheral neuropathy or spinal cord damage.

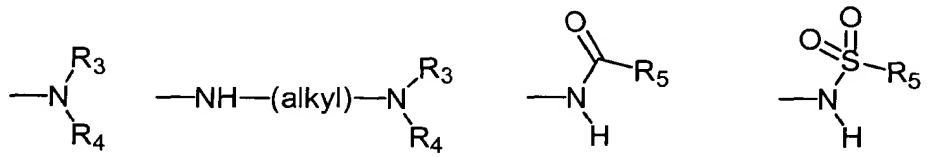
30. (New) A method for inhibiting JNK in a cell capable of expressing JNK, comprising contacting said cell with an effective amount of a compound having the structure:



or a pharmaceutically acceptable salt thereof,

wherein

R_1 and R_2 are optional substituents that are the same or different and independently represent alkyl, halogen, nitro, trifluoromethyl, sulfonyl, carboxyl, alkoxycarbonyl, alkoxy, aryl, aryloxy, arylalkyloxy, arylalkyl, cycloalkylalkyloxy, cycloalkyloxy, alkoxyalkyl, alkoxyalkoxy, aminoalkoxy, mono- or di-alkylaminoalkoxy, or a group represented by formula (a), (b), (c) or (d):

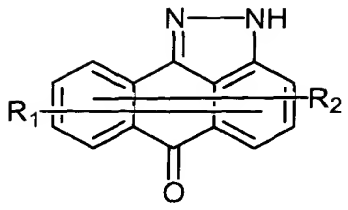


(a) (b) (c) (d)

R_3 and R_4 are the same or different and independently represent hydrogen, alkyl, cycloalkyl, aryl, arylalkyl, cycloalkylalkyl, aryloxyalkyl, alkoxyalkyl, alkoxyamino, or alkoxy(mono- or di-alkylamino); and

R_5 represents hydrogen, alkyl, cycloalkyl, aryl, arylalkyl, cycloalkylalkyl, alkoxy, amino, mono- or di-alkylamino, arylamino, arylalkylamino, cycloalkylamino, or cycloalkylalkylamino.

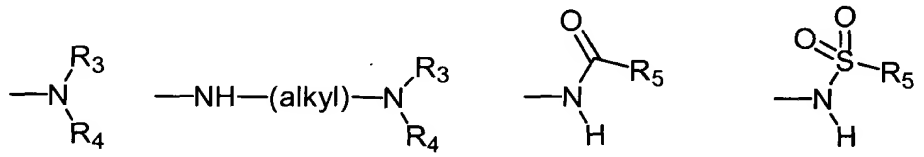
31. (New) A method for inhibiting JNK, comprising contacting JNK with an effective amount of a compound having the structure:



or a pharmaceutically acceptable salt thereof,

wherein

R_1 and R_2 are optional substituents that are the same or different and independently represent alkyl, halogen, nitro, trifluoromethyl, sulfonyl, carboxyl, alkoxycarbonyl, alkoxy, aryl, aryloxy, arylalkyloxy, arylalkyl, cycloalkylalkyloxy, cycloalkyloxy, alkoxyalkyl, alkoxyalkoxy, aminoalkoxy, mono- or di-alkylaminoalkoxy, or a group represented by formula (a), (b), (c) or (d):



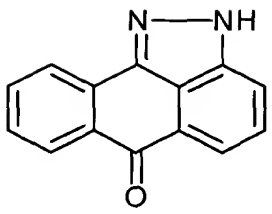
(a) (b) (c) (d)

R_3 and R_4 are the same or different and independently represent hydrogen, alkyl, cycloalkyl, aryl, arylalkyl, cycloalkylalkyl, aryloxyalkyl, alkoxyalkyl, alkoxyamino, or alkoxy(mono- or di-alkylamino); and

R_5 represents hydrogen, alkyl, cycloalkyl, aryl, arylalkyl, cycloalkylalkyl, alkoxy, amino, mono- or di-alkylamino, arylamino, arylalkylamino, cycloalkylamino, or cycloalkylalkylamino.

32. (New) The method of claim 9, 30 or 31, wherein the JNK is JNK1, JNK2 or JNK3.

33. (New) The method of claim 28, 30 or 31, wherein the compound has the structure:



or a pharmaceutically acceptable salt thereof.

34. (New) The composition of claim 8 or 24, wherein the composition is a pharmaceutical composition.

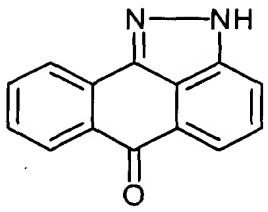
35. (New) The composition of claim 8 or 24, wherein the compound or pharmaceutically acceptable salt of the compound is present in an amount that is effective for inhibiting JNK.

36. (New) The composition of claim 8 or 24, wherein the compound or pharmaceutically acceptable salt of the compound is present in an amount that is effective for treating cancer; rheumatoid arthritis; rheumatoid spondylitis; osteoarthritis; gout; asthma; bronchitis; cystic fibrosis; inflammatory bowel disease; irritable bowel syndrome; mucous colitis; ulcerative colitis; Crohn's disease; gastritis; esophagitis; hepatitis; multiple sclerosis; endotoxin shock; psoriasis; eczema; dermatitis; atherosclerosis; restenosis following angioplasty; left ventricular hypertrophy; myocardial infarction; stroke or ischemic damage to the heart, kidney, liver, or brain; transplant rejection; or a central or peripheral neurological degenerative disorder.

37. (New) The composition of claim 36, wherein the central or peripheral neurological degenerative disorder is epilepsy, Alzheimer's disease, Parkinson's disease, Huntington's disease, amyotrophic laterial sclerosis, a peripheral neuropathy or spinal cord damage.

38. (New) The composition of claim 34, wherein the composition is in the form of a pill, tablet or capsule.

39. (New) A composition comprising JNK and a compound having the structure:



or a pharmaceutically acceptable salt thereof, wherein the compound is present in an amount effective for inhibiting JNK.